the cell body. Thus, transcripts in the neuropil are more likely to be monosome-associated than are somatic transcripts.

To assess any effects of ribosome occupancy on protein levels, the authors performed mass spectrometry analysis on neuropil to estimate absolute protein levels. Although proteins encoded by polysome-preferring transcripts were more abundant than proteins encoded by monosome-preferring transcripts, this correlation was weak: only 177 of the 326 monosome-preferring transcripts encoded protein that was more abundant than average. Moreover, some of these monosome-preferring transcripts encoded proteins that were highly abundant in the neuropil, and these transcripts generally tended to be locally abundant and translated at a high rate. Therefore, monosome-preferring transcripts can be translated to produce proteins with low or high abundance.

Credit: Jennie Vallis/Springer Nature Limited

Together, these data suggest that monosomes may preferentially translate certain transcripts, particularly in the neuropil, and that this mode of translation is an important source of synaptic proteins.

Natasha Bray

ORIGINAL ARTICLE Biever, A. et al. Monosomes actively translate synaptic mRNAs in neuronal processes. *Science* **367**, eaay4991 (2020)

that, unlike primary cells, organoid cells co-expressed radial glia and neuronal markers, suggesting dysregulated radial glia–neuron maturation. Moreover, organoid cells showed increased expression of glycolysis and endoplasmic reticulum (ER) stress genes and a lack of upregulation of genes associated with neuronal maturation and projection patterning compared with the primary cells.

The authors used scRNA-seq to investigate whether areal signatures of cortical excitatory neurons were preserved in organoids. They found that, although most organoid neurons could be matched to a specific, known areal signature, they were present as a heterogeneous mixture in organoid tissue and lacked spatial organization.

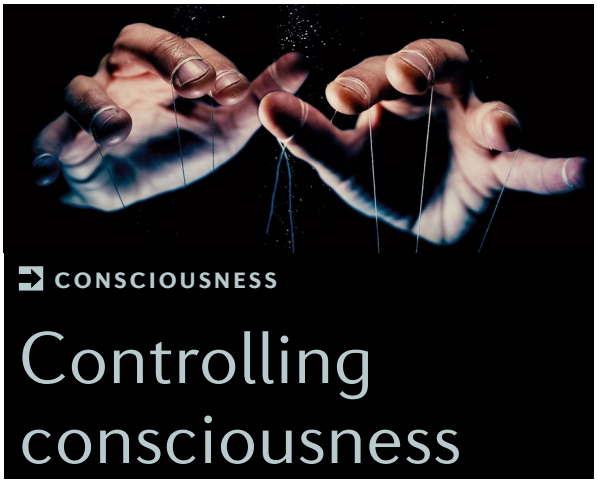
Genes associated with metabolic stress are enriched in organoid cells. There is little expression of stress genes during normal cortical development, so their expression in organoids could be a consequence of in vitro culture conditions. Indeed, these genes were upregulated in PSCs. Furthermore, stress genes in primary cortical cells were upregulated when the authors transplanted them into organoids. ER stress can inhibit cell-type specification, and the authors found that the transplanted primary cells showed reduced expression of neuronal or progenitor subtype marker genes — similar to organoid cells.

Last, the authors transplanted human organoid neurons into the cortices of postnatal day 4 mice. Five weeks after transplantation, scRNA-seq analysis showed that post-transplantation organoid-derived cells showed a substantial reduction in stress-marker expression. When isolated from the mouse cortex, these cells showed a greater capacity for specification to outer radial glia and newborn neurons than did non-transplanted organoid-derived cells.

Together, these data suggest that metabolic stress could contribute to the dysregulation of cell differentiation in organoid cultures.

Sian Lewis

ORIGINAL ARTICLE Bhaduri, A. et al. Cell stress in cortical organoids impairs molecular subtype specification. *Nature* **578**, 142–148 (2020)



Credit: Spencer_Whalen/Getty

CONSCIOUSNESS

Controlling consciousness

Neuroscientists have long sought to identify the mechanisms required for conscious experience. In their new paper, Redinbaugh et al. show that, in macaques, the central lateral thalamus (CL) has a key role in the control of consciousness, through the modulation of specific corticocortical pathways.

Consciousness is thought to involve feedforward and feedback interactions between cortical layers and areas. As the CL is connected to both superficial and deep cortical layers, it is well-positioned to modulate consciousness. Here, electrical stimulation of the CL in two anaesthetized macaques generated temporary behavioural indications of arousal, including face and body movements typical of wakefulness.

To further examine the CL's role in consciousness, the authors simultaneously recorded neural activity in the CL and in two reciprocally connected cortical areas — the lateral intraparietal area (LIP) and the frontal eye field (FEF) — in response to an auditory stimulus. Sleep and anaesthesia were associated with less activity in the CL and in deep layers of the LIP and FEF than wakefulness, whereas CL stimulation reversed these changes.

Next, the authors considered how changes in consciousness state relate to interactions between and within these brain areas. Both anaesthesia and sleep were associated with a decreased coherence of alpha and gamma band oscillations in activity between deep and superficial layers within each cortical area, in comparison with wakefulness or CL stimulation. Similarly, there was a decrease in alpha and gamma coherence between the LIP and FEF and between the CL and the cortex under anaesthesia and during sleep. CL stimulation restored alpha and gamma coherence in a feedforward pathway between superficial layers of the LIP and superficial and middle layers of the FEF, and restored alpha coherence in feedback pathways projecting from the deep layers of the FEF to the LIP.

This study provides evidence for the involvement of intracolumnar and long-range corticocortical pathways in conscious experience and suggests that the CL has an essential role in driving these interactions. These findings could eventually contribute to the treatment of disorders of consciousness.

Katherine Whalley

ORIGINAL ARTICLE Redinbaugh, M. J. et al. Thalamus modulates consciousness via layer-specific control of cortex. *Neuron* https://doi.org/10.1016/j.neuron.2020.01.005 (2020)